REMARKS

I. Introduction

It is respectfully requested that this Amendment After Final Rejection be entered and made of record. It is believed that the following amendments and remarks place the application in a form for allowance. The following amendments and remarks at least place the claims in a better form for appeal. No new matter is presented, as such the amendment is proper under 37 C.F.R. § 1.116.

II. Status of the Claims

Applicants have now canceled claims 3, 5-6, 9-11, 13, and 15-16 from the application, and added new claims 17-18 which depend from claim 1. Thus, only claims 1 and 17-18 are remaining in the case. Claim 1 has been amended in a sincere effort to place the application in allowable form.

III. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 1, 5, 6, 9-11, and 15 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Specifically, the Examiner states that the use of the term "peptide" in the claims is indefinite on the basis that the specification has differing meanings for the term, thus leading to confusion as to the scope of the claims.

Applicants have now amended claim 1 to incorporate the specific peptides of claim 3 (now canceled), as suggested by the Examiner. Claims 5, 6, 9-11, and 15 have been canceled. It is therefore believed this ground of rejection has been alleviated.

IV. Claim Rejections - 35 U.S.C. § 102

A. Groves et al.

Claims 1, 5-6, 10-11, and 15-16 were rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Groves et al. Claim 1 has now been amended to include the specific peptides set forth in claim 3, now canceled. Since claim 3 was not part of the Examiner's anticipation rejection, it is respectfully submitted that claim 1 is not anticipated by Groves et al.

Claims 5-6, 10-11, and 15-16 have been canceled, thereby rendering the ground of rejection with respect to these claims moot.

B. Thiemermann et al.

Claims 1, 5, 9-11, and 15 were rejected under 35 U.S.C. § 102(b) as being anticipated by Thiemermann et al. As already noted, claim 1 has been amended to include the specific peptides set forth in claim 3, now canceled. Since claim 3 was not part of the Examiner's anticipation rejection, it is respectfully submitted that claim 1 is not anticipated by Thiemermann et al. Claims 5, 9-11, and 15 have been canceled, thereby rendering the ground of rejection with respect to these claims moot.

C. U.S. Pat. No. 4,585,757

Claims 1, 3, 5-6, 9-11, and 15-16 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 4,585,757 ("the '757 patent"). Claim 1 has been amended to include the provisions of claim 10, now canceled, that the method is used to treat a nitric oxide-mediated disease using the specific peptides set forth in claim 13, also now canceled. Since claim 13 was not part of the Examiner's anticipation rejection, it is respectfully submitted that claim 1 is not anticipated by the '757 patent. Claims 3, 5-6, 9-11, and 15-16 have been canceled, thereby rendering the ground of rejection with respect to these claims moot.

D. U.S. Pat. No. 6,143,719

Claims 1, 3, 5-6, 9-11, and 15-16 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Pat. No. 6,143,719 ("the '719 patent"). Claim 1 has been amended to include the provisions of claim 10, now canceled, that the method is used to treat a nitric oxide-mediated disease using the specific peptides set forth in claim 13, also now canceled. Since claim 13 was not part of the Examiner's anticipation rejection, it is respectfully submitted that claim 1 is not anticipated by the '719 patent. Claims 3, 5-6, 9-11, and 15-16 have been canceled, thereby rendering the ground of rejection with respect to these claims moot.

V. Claim Rejections - 35 U.S.C. § 103

A. U.S. Pat. No. 4,152,425

Claims 1, 3, 5-6, 9-11, 13, and 15-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 4,152,425 ("the '425 patent"). The '425 patent discloses the infusion of 100-600 grams of glucose and 10-3000 μg of kinin/l solution for intravenous feeding.

Claim 1 has now been amended to provide that Applicants' method is used in a therapeutically effective amount to treat a nitric oxide-mediated disease. Support for this amendment is found on page 27, fourth paragraph, lines 17-18 in particular. No new matter has been added. Thus, Applicants' method requires an amount and dosing schedule of peptide sufficient to treat or prevent nitric oxide-mediated disease. This is in contrast to the method of the '425 patent which requires an amount of kinin sufficient for feeding purposes. There is no teaching or motivation in the '425 patent to modify its methods to infuse a nitric oxide-mediated disease treatment effective amount of bradykinin or other kinins to treat disease. Claim 1 and new claims 17-18 which depend from claim 1 are therefore not obvious in view of the '425 patent. Since claims 3, 5-6, 9-11, 13, and 15-16 have been canceled, the rejection with respect to these claims is rendered moot.

New claim 19 has also been added which is directed to the method of treating nitric oxide-mediated diseases consisting essentially of administering a therapeutically effective amount of Applicants' specific peptides. The partially-closed language "consisting essentially of" in the preamble of claim 19 prevents the inclusion of ingredients that would destroy the basic and novel characteristics of the claimed invention, and therefore precludes the addition of the glucose required in the composition and method of the '425 patent. Thus, claim 19 is also not rendered obvious by the '425 patent.

B. U.S. Pat. No. 5,648,333

Claims 1, 5-6, 9-11, and 15-16 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 5,648,333 ("the '333 patent). As noted above, claim 1 has been amended to include the provisions of claim 10, now canceled, that the method is used to treat a

nitric oxide-mediated disease using the specific peptides set forth in claim 13, also now canceled. Since claim 13 was not part of the Examiner's anticipation rejection, it is respectfully submitted that claim 1 is not rendered obvious by the '333 patent. Claims 5-6, 9-11, and 15-16 have been canceled, thereby rendering the ground of rejection with respect to these claims moot.

VI. Conclusion

For the above reasons, it is believed that the present application is in a condition for allowability. Allowance is respectfully requested.

A check for $205.00 for a two month extension of time is attached. Any deficiency or overpayment should be charged or credited to Deposit Account 26-0084.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

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AMENDMENT — VERSION WITH MARKINGS TO SHOW CHANGES MADE — DO NOT FILE

In the Claims

Claim 1 has been amended as follows.

1. (Twice Amended)

A method of [regulating or controlling nitric oxide production] preventing or treating a nitric oxide-mediated disease or condition in a mammalian subject comprising administering to the mammal [from about 20-500 μg/kg] a disease or condition prevention or treatment effective amount of a peptide, oligopeptide, or protein that acts as a substrate for or an inhibitor of nitric oxide synthase, whereby the tertiary structure of the peptide, oligopeptide, or protein inhibitor is such that one or more arginine groups are available to the nitric oxide synthase, said peptide, oligopeptide or protein being selected from the group consisting of L-Arginine, Poly-Arginine, BK, Des-Arg1-BK, Des-Arg9-BK, BK fragment 1-7, BK fragment 2-7, [Lys1]-BK, Lys-BK, Ile-Ser-BK, and Met-Lys-BK.

Claims 3, 5-6, 9-11, 13, and 15-16 have been canceled.

New claims 17-19 have been added:

17. (New)

The method of claim 1 wherein the disease or condition relates to a cardiovascular, gastrointestinal, or bronchial disorder.

18. (New)

The method of claim 17 wherein the disease or condition is selected from the group consisting of ischemic stroke, diabetes, systemic hypotension, multiple sclerosis, Huntington's disease, Parkinson's disease, and Alzheimer's disease.

19. (New)

A method of preventing or treating a nitric oxide-mediated disease or condition in a mammalian subject consisting essentially of administering to the mammal a disease of condition prevention or treatment effective amount of a peptide, oligopeptide, or protein that acts as a substrate for or an inhibitor of nitric oxide synthase, whereby the tertiary structure of the peptide, oligopeptide, or protein inhibitor is such that one or more arginine groups are available to the nitric oxide synthase, said peptide, oligopeptide or protein being selected from the group consisting of L-Arginine, Poly-Arginine, BK, Des-Arg1-BK, Des-Arg9-BK, BK fragment 1-7, BK fragment 2-7, [Lys1]-BK, Lys-BK, Ile-Ser-BK, and Met-Lys-BK.